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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/622,439	08/17/00	MATSUMOTO	M Q60438

EXAMINER
WEGERT, S

ART UNIT	PAPER NUMBER
1647	9

DATE MAILED: 04/25/01

HM22/0425

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Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary	Application No.	Applicant(s)	
	09/622,439	MATSUMOTO ET AL.	
	Examiner	Art Unit	
	Sandra Wegert	1647	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *28 February 2001* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-8* is/are pending in the application.

4a) Of the above claim(s) *1,2,7,8* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *3-6* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claims *1-8* are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

13)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

15) ☒ Notice of References Cited (PTO-892)
16) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
17) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
18) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
19) ☐ Notice of Informal Patent Application (PTO-152)
20) ☐ Other: .

DETAILED ACTION

Formal Matters

Status of Application, Amendments, and Claims:

The 10 sheets of formal drawings (Paper 6, filed 11/27/00), and the Election/Preliminary Amendment (Paper 7, filed 2/28/01) have been entered into the record.

Applicant's election of Group II, claims 3-6, in Paper No. 7, and Group B (SEQ ID NO:4) is acknowledged.

Claims 1-2 and 7-8 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected Invention, there being no allowable generic or linking claim.

The Preliminary Amendment submitted 2/28/01 (Paper 7) amended claims numbered 3-6. The Preliminary Amendment submitted 4/09/01 (Paper 9) modified claim 5. Claims 3-6 are under examination in the current application.

Title

The title of the invention is not descriptive. A new title is required that is clearly indicative of the invention to which the claims are directed. The following title is suggested: "POLYNUCLEOTIDES ENCODING SREB2 RECEPTOR".

Appropriate correction is required.

Specification

The disclosure is objected to because of the following informalities:

Applicant has not complied with one or more conditions for receiving the benefit of an earlier filing date under 35 U.S.C. 371 as follows: An application in which the benefits of an

earlier application are desired must contain a specific reference to the prior application(s) in the first sentence of the specification (37 CFR 1.78).

Appropriate correction is required.

The disclosure is objected to because it contains figures that are not properly labeled. Fig. 11 and Fig. 12 contain graphs in which the units on the Y-axes are not specified.

Appropriate correction is required.

The disclosure is objected to because it contains Brand Names of products without accompanying indications of Trademark or Copyright: for example on p.31, line 16. Brand names should be listed in Capital Letters, followed by a "©", "®" or "™" symbol, and a short generic description in parentheses. See MPEP § 608.01 (v).

Appropriate correction is requested.

Abstract

The abstract fails to comply with the provisions of MPEP 608.01(b) in that there are two abstracts, of more than one paragraph each. There must be only one abstract, containing one paragraph of 25 lines or less and 250 words or less.

Appropriate correction is required.

Sequence Rules

The instant application is not fully in compliance with the sequence rules, 37 CFR 1.821-1.825, because each disclosure of a sequence embraced by the definitions set forth in the rules is not accompanied by the required reference to the relevant sequence identifier (i.e., SEQ ID NO:). This occurs throughout the disclosure, but see for example: p. 8, line 13, line 18, line 21; p. 9, line 2; and p. 10, line 10.

Appropriate correction is required.

Claim Rejections - 35 USC § 101 and 35 USC § 112, first paragraph

35 U.S.C. 101 reads as follows:

Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 3-6 are rejected under 35 U.S.C. 101 because the claimed invention is not supported by either a credible, specific and substantial asserted utility or a well-established utility.

The claims are directed to a nucleotide and expression system encoding a SREB2 receptor which resembles in general structure numerous other "7TM" G-protein-coupled receptors.

The "SREB2" receptor is an "orphan" receptor, meaning that no ligand is known for the receptor and no function has been attributed to it. The instant specification suggests similarities to the G-protein-coupled family of receptors, a family containing numerous and diverse members. However, the specification does not disclose the function of the receptor in the context of the cell or organism. The applicant does not disclose any modulatory function, any endogenous ligands, nor any diseases or conditions associated with altered levels or forms of the SREB2 peptide or its putative ligands. Significant further experimentation would be required of the skilled artisan to identify *any* function associated with this peptide.

No well-established utility exists for newly isolated complex biological molecules. However, the specification asserts the following as credible, specific and substantial patentable utilities for the putative ligand polypeptide encoded by the claimed polynucleotide:

1) to make antibodies to the SREB2 receptor polypeptides.

2) in assays that screen for compounds capable of changing the *SRE* or *CRE* response elements.

Each of these shall be addressed in turn:

1) to make antibodies to the polypeptide receptor. This asserted utility is credible and substantial, but not specific. Antibodies can be made to any polypeptide. However, if the specification discloses nothing specific and substantial about the polypeptide, both the polypeptide and its antibodies have no patentable utility.

2) in assays screening for compounds capable of changing the SRE or CRE response elements. This asserted utility is also credible and substantial but not specific. Such can be performed for many G-protein-coupled receptors. Additionally, the specification discloses nothing specific or substantial for the compounds that can be identified by this method.

Claims 3-6 are also rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a specific and substantial asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention.

Claims 3-6 are directed to a polynucleotide coding for the G-protein coupled receptor of SEQ ID NO:4. Further, the claims recite an expression vector comprising the nucleic acid molecule that produces the polypeptide having the amino acid sequence of SEQ ID NO:4, a recombinant host cell, and a process of producing a recombinant host cell and polypeptide.

The specification teaches a receptor having characteristics of the large family of G protein-coupled receptors, such as: seven putative plasma membrane-spanning regions, as well as probable intervening non-helical "loop" regions. This similarity to G protein-coupled receptors combined with brain and testis-specific expression patterns of SREB2 indicates a probable function for this receptor.

Generally, the art acknowledges that function cannot be predicted based solely on structural similarity to a protein found in the sequence databases. For example, Skolnick et al. (2000, Trends in Biotech. 18:34-39) state that knowing the protein structure by itself is insufficient to annotate a number of functional classes, and is also insufficient for annotating the specific details of protein function (see Box 2, p. 36). Similarly, Bork (2000, Genome Research 10:398-400) states that the error rate of functional annotations in the sequence database is considerable, making it even more difficult to infer correct function from a structural comparison of a new sequence with a sequence database (see especially p. 399). Such concerns are also echoed by Doerks et al. (1998, Trends in Genetics 14:248-250) who state that (1) functional information is only partially annotated in the database, ignoring multi functionality, resulting in underpredictions of functionality of a new protein and (2) overpredictions of functionality occur because structural similarity often does not necessarily coincide with functional similarity. Smith et al. (1997, Nature Biotechnology 15:1222-1223) remark that there are numerous cases in which proteins having very different functions share structural similarity due to evolution from a common ancestral gene. Brenner (1999, Trends in Genetics 15:132-133) argues that accurate inference of function from homology must be a difficult problem since, assuming there are only about 1000 major gene superfamilies in nature, then most homologs must have different molecular and cellular functions. Finally, Bork et al. (1996, Trends in Genetics 12:425-427) add that the software robots that assign functions to new proteins often assign a function to a whole

new protein based on structural similarity of a small domain of the new protein to a small domain of a known protein. Such questionable interpretations are written into the sequence database and are then considered facts.

Therefore, based on the discussions above concerning the specific examples of structurally similar proteins that have different functions, along with the art's recognition that one cannot rely upon structural similarity alone to determine functionality, the specification fails to teach the skilled artisan how to use the claimed polynucleotides to make biologically active SREB2 without resorting to undue experimentation to determine what the specific biological activities of the polypeptide are.

The specification does not teach the skilled artisan how to use the claimed polynucleotides encoding SREB2 for purposes unrelated to the asserted biological activity. For example, there is no disclosure of particular disease states correlating to an alteration in levels or forms of the polypeptide such that the claimed nucleotide encoding SREB2 receptor could be used as a diagnostic tool. Therefore, the skilled artisan is not provided with sufficient guidance to use the claimed polynucleotides for any purpose.

Due to the large quantity of experimentation necessary to determine an activity or property of the disclosed polypeptide such that it can be determined how to use the claimed polynucleotides encoding SREB2 and to screen for activity, the lack of direction/guidance presented in the specification regarding same, the absence of working examples directed to same, the complex nature of the invention, the state of the prior art establishing that biological activity cannot be predicted based on structural similarity and the unpredictability of the effects of mutation on protein structure and function, and the breadth of the claims which fail to recite particular biological activities and also embrace a broad class of structural fragments and

variants, undue experimentation would be required of the skilled artisan to make and/or use the claimed invention in its full scope.

Claim Rejections – 35 USC § 102

The following is a quotation of the appropriate paragraph of 35 USC § 102 that form the basis for rejections under this section:

> **(e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.**

Claims 3-6 are rejected under 35 USC § 102 (e) as being anticipated by Elshourbagy et al in US Patent 6,071,722. Claim 3 is drawn to a polynucleotide encoding the peptide of SEQ ID NO:4. Claim 4 is drawn to an expression vector for producing the polypeptide of claim 3. Claim 5 is drawn to the host cell containing the vector of claim 4. Claim 6 is drawn to a process for producing a recombinant host cell.

Elshourbagy et al -in US Patent 6,071,722-, teach how to make and use a 7TM receptor, which they refer to as "AXOR1" (Ref. A, enclosed). They also teach the polynucleotide sequence of the "AXOR1", which is 100% identical to the nucleotide encoding SEQ ID NO:4 of the instant application. Ref. A also teaches an expression vector comprising a polynucleotide encoding a polypeptide having 100% identity to SEQ ID NO:4, as well as a method of recombination for expressing same. They express the "AXOR1" receptor by means of HEK293 or adherent CHO cells (col. 18, line 23) with described vectors and selection methods. Ref. A also contains examples wherein levels of expression are measured as well as teaches several functional assays (col. 18-20).

Conclusion

No claims are allowed.

A shortened statutory period for reply to this action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Advisory information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sandra Wegert whose telephone number is (703) 308-9346. The examiner can normally be reached Monday - Friday from 8:30 AM to 5:00 PM (Eastern Time).

If attempts to reach the examiner by telephone are unsuccessful, the Examiner's supervisor, Gary Kunz, can be reached at (703) 308-4623.

Official papers filed by fax should be directed to (703) 308-4242. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Elizabeth C. Kemmerer

SLW

April 16, 2001

ELIZABETH KEMMERER
PRIMARY EXAMINER